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and follow the assistant's instructions.

Topics/Questions for Discussion for SPL ER/DL Process Team – 13-Dec-17

1. If someone needs to be added to the email list, please have them reach out to both Herb and I.
 - a. Benjamin.E.Harpster@gsk.com
 - b. Herbert.Obrien@bayer.com
2. (Shared Learning) Jean Lensing of Abbvie – Noticed that some of the “manufactured under contract” listings were appearing on DailyMed. Received this response from Lonnie:

Greetings,

Please provide the DailyMed links.

Please note that initially some of the files were erroneously posted but the FDA IT staff should have prevented others from being posted.

The follow up email from Lonnie states that it will be removed by the end of the year.

Follow-up from Amanda Broughton at Jubilant HolisterStier

“Approved Drug Manufactured Under Contract” and “Drugs for Further Processing” listings were also posted in both the NDC directory & NDC unfinished drugs database. EDRLS Staff answered that they are working on the issue and expect it to be implemented in the next release around Dec. 25.

3. (Shared Learning) Amanda Broughton – Jubilant HolisterStier
 - a. For those that did not know, “Licensed Vaccine Bulk Intermediate” is the equivalent of “Drugs for Further Processing” listing, but for a vaccine product.
 - b. This was verified by Lonnie.
4. Sandra Kuhn – Janssen
 - a. We have a product that has three different formulations included in one SPL. We have withdrawn the NDA for one of the formulations and updated the market end date. Once the product is delisted, do companies remove the principle display panel from the SPL or does it continue to be included in the SPL.

Answer: I don’t remove anything from the SPL until the last lot expiry has passed for the discontinued sku(s). Once that date has passed, on the next update I will remove whatever I can. In the above scenario, I would remove the applicable PDP, the applicable Product Data Elements info, and any reference to the product code in the Labeler/Manu section. How supplied would also be updated. Anyone handle it differently?

5. Amanda Broughton – Jubilant HolisterStier
 - a. How do you find out the registrant information for a product you make for another company where their drug listing has that information confidential?

Answer: Contact the company you are making the drug for and find out what they want to use. If they won’t provide it, then I would either enter the labeler info or leave it blank. Anyone have another suggestion?

Discussion: Only documentation available for specific information about the registrant inclusion in drug listing files is in the Step-by-Step Instructions. This document indicates that the registrant data field should be used by the manufacturer of the drug when the labeler is the private label distributor and the manufacturer is submitting on behalf of the PLD. Otherwise this field is left blank. There is no validation check on this data field. If the labeler and the registrant are the same, this field is typically left blank. NDA/BLA holders that are not manufacturing the product are not to be included in this submission. Ben Harpster will reach out to Lonnie Smith to confirm and clarify this information.

See Section 4.4 - Step-by-Step Instructions for Creating Structured Product Labeling (SPL) Files for Drug Establishment Registration and Drug Listing:
<https://www.fda.gov/downloads/ForIndustry/DataStandards/StructuredProductLabeling/UCM162027.pdf>

Additional relevant comments for PLD drugs are made here:

<http://spl-work-group.wikispaces.com/file/view/20110330+Min+DRLS+Import+CMV.pdf>

6. Kerrin Bright – RB

Scenario:

The first facility (Establishment A) is a foreign establishment manufacturing tablets.

Tablets are then imported as bulk drums into the US to a second facility (Establishment B).

The second facility (Establishment B) is within the US and packs tablets from bulk drums into blister packs, packaged in bulk.

Bulk blister packs are then transported to a third facility (Establishment C) where they are placed into cartons as finished product for commercial distribution.

Finished product is drug listed including all establishments that participate in an operation interpreted as part of the business operation/manufacturing process (pack, analysis, manufacturer, etc.).

Question:

Is there any need to drug list the blister packs, packaged in bulk, being transported from Establishment B to Establishment C?

Discussion:

If all registered establishments are owned by the same company, the transaction is considered an interplant shipment and separate drug listings are not necessary for each establishment. Internal or interplant transactions include transfer between registered establishments under common ownership and control, including a parent, subsidiary, or affiliate company. Further, each registered establishment should be included in the drug listing made for commercial distribution with indication of the business operation/manufacturing process (pack, analysis, manufacturer, etc.) taking place at each establishment. This listing is made under the company's labeler code including the company as the labeler and the manufacturer of the product. This submission will also include a Data Elements section and full Content of Labeling section.

If the registered establishments are owned by different parent companies, then the transactions between those establishments which are owned by the different parent companies should be accounted for; i.e. a drug listing submission would then be necessary in addition to the above-mentioned submission. In addition to the submission made for commercial distribution, submissions should then also be made under the appropriate marketing category (drug for further processing) by each parent company including the associated business operations/manufacturing process taking place at those establishments. These submissions are not made public and are for FDA tracking purposes only. These submissions would be made under the respective company's labeler code including that company as the labeler and the registered establishment. These submissions would include a Data Elements section and a Content of Labeling section including

the representative image of the product labeling at that point in the product life cycle, i.e. shipping label.

Further clarification from FDA may be necessary. Additional relevant discussion can be found here:

<http://spl-work-group.wikispaces.com/file/view/20110330+Min+DRLS+Import+CMV.pdf>

7. Additional scenarios and discussions

Scenario:

Company X owns Establishment A and Company Y owns Establishment B. Company X is the owner of the product.

Company X manufactures unfinished tablets at Establishment A. Company Y performs a business operation on the tablets (enrobing the tablets) at Establishment B as part of the manufacturing process. The enrobed tablets are then shipped back to Company X at Establishment A to be placed in packaging for final distribution.

Discussion:

Because the transactions between the two registered establishments are not interplant transfers, the transactions between Establishment A and Establishment B should be accounted for by the submission of a listing. These submissions, detailed below, are made under the marketing category “drug for further processing” and should indicate the business operations/manufacturing processes performed on the product at that establishment.

A listing for Company X will be made as the labeler and registered establishment of the product under the appropriate marketing category for distribution (monograph citation, NDA, etc.) and under their own labeler code. This submission will be made public and is the submission made for commercial distribution. Each registered establishment will be included in this submission indicating what operations are performed at that establishment. This submission will also include a Data Elements section and a full Content of Labeling section.

A listing for Company Y will be made under their own labeler code. In this submission Company Y is the labeler and the registered establishment, indicating the operation being performed on the product, and using the marketing category “drug for further processing.” This submission is not made public and is for FDA tracking purposes only. This submission will include a Data Elements section and a Content of Labeling section including the PDP (shipping label).

Scenario:

Company A is a foreign company.

Company A is the NDA holder for the product and is marketing this product.

Company A has contracted Company B to manufacture the product.

Company B is a foreign establishment and is the contract manufacturer.

Company C is a domestic establishment and handles the physical distribution of the product.

Company B imports the product into the US for packaging and labeling at the domestic establishment of Company C.

The product is then physically distributed by Company C, from the domestic establishment owned by Company C.

The product has been held in customs upon importation.

All of the establishments are owned by different companies and establishment registrations were submitted accurately. It is important to note that if Company A is only the NDA holder (sponsor), then no establishment registration or listing is required. Registration and listing requirements only pertain to manufacturing establishments and distributors.

Company B has submitted the appropriate drug listing.

For the release of the product from Customs, the FDA Compliance Officer at the port is requesting:

- drug listing made by Company C under the Company C labeler code
- drug listing made by Company A with the packaging and labeling information

Discussion:

Company A is selling/marketing the product under the marketing category "NDA". A listing should be submitted under the Company A labeler code with both Company B and Company C included as the establishments. Relevant business operations/manufacturing processes should be identified for the establishments. Because Company A is the seller of the product, the listing is being requested by the FDA Compliance Officer at the port.

If Company A was merely the NDA holder (sponsor) for the product, but not marketing the product for commercial distribution, no registration or listing requirements would be applicable.

From the scenario on the call, it is more than likely that Company A is not only the NDA holder because the FDA Compliance Officer is requesting a drug listing from Company A along with packaging and labeling. Further, the caller stated that Company A is selling the product. This listing will be made public and includes a completed Data Elements and Content of Labeling section. The final packaging/label is the PDP. This listing is to be made by either Company A or Company C; however, Company C is acting in a manufacturing role and is ultimately responsible for the listing.

A listing for Company B should be made for the product under Company B labeler code using the marketing category (drug manufactured under contract previously drug manufactured exclusively for PLD, drug for further processing, etc.) and indicating business operations/manufacturing processes performed at that establishment. This listing should include Company B listed as the labeler and establishment. This listing is not made public and is for FDA tracking purposes only. This listing should include a completed Data Elements section and PDP for the packaging of the product in the Content of Labeling. Since this product is not packaged at this point for final distribution, the shipping label should be included as the PDP along with relevant NDC numbers.

A listing for Company C should be made for the product under the Company C labeler code using the appropriate marketing category (drug manufactured under contract) and indicating the business operations/manufacturing process performed at that establishment. Company C is listed as the labeler and as the establishment in this listing. Company C is an establishment in this listing that is packaging and labeling the product. This listing should include a completed Data Elements section and PDP for the packaging of the product in the Content of Labeling. Since the product is packaged in the final packaging at this point, the PDP should include an image of the final packaging of the product.

EDRLs confirms that the listings requested at Customs by the FDA Compliance Officer are necessary for product release.

FDA requests information of all transactions of the product during the manufacturing cycle. Because in this scenario, not all transactions have been accounted for, the product is being held. While separate listings are not required to account for interplant transactions where products are transferred from one facility to another within the same company; each facility should still be registered and included in relevant listings along with the business operation/manufacturing processes taking place at that facility. FDA is now using the port of entry as a place to confirm all the appropriate listings and registrations have been submitted throughout the product life cycle for both foreign and domestic facilities.

In the scenarios above, a quality agreement can be a useful tool for delegating responsibility for registration and listing requirements between companies. Additional details of such an agreement

could further outline the processes by which the requirements are met and verified between companies. It is important to note that ultimately the manufacture(s) of the product are responsible for registration and listing; however, the distributor can elect to do their own listings.

This document pertains to quality agreements in the contract manufacturing arrangement:

<https://www.fda.gov/downloads/drugs/guidances/ucm353925.pdf>

Question from Steve Rock: (tabled until next call or via email)

When attempting to do an annual recertification for the drug products with a confidential establishment, the products do not show up under the labeler so you can't recertify them using the blanket no changes certification.

When you complete an annual recertification, and look at the exported SPL it's a very simple SPL showing only the establishments and their FEIs. There are no drug products included in the SPL. It's impossible to say which products were recertified by looking at the exported recertification SPL.

If you want to recertify drug products with a confidential establishment, can you do so by creating and uploading a recertification SPL, listing the confidential establishment and their FEI in the same format as an exported recertification SPL?

If so, how do you know whether or not uploading the SPL actually recertifies any products?

Question:

New UNII requests/identification are still being sent to the FDA Substance Registration System at:

FDA-SRS@fda.hhs.gov

Shared FDA response:

Here is what I sent to Lonnie for clarification:

During the SPL process meeting a topic came up that we couldn't agree on. For the registrant in the Labeler/Manu section of the drug listing, who should that be? Here are the answers that we had:

1. If you are drug listings something on behalf of another company, then you would list yourself as the registrant as you are submitting the drug listing.

2. The NDA/BLA holder is the registrant. If the NDA/BLA holder and the Labeler are the same, then you can leave the registrant blank.

Here is his response:

“4.4 Registrant

“The registrant is included if they are listing a drug made for a private label distributor. The information includes the name and DUNS Number. Otherwise, this is blank.”

Note: By “blank,” it means delete the empty registrant data elements in the product SPL file.

Shared by Marcia Howard – Federal Register notices.

Published October 20, 2017 – Link to FR notice + summary except

- <https://www.gpo.gov/fdsys/pkg/FR-2017-10-20/pdf/2017-22768.pdf> FDA Extension of the Timetable Requirement to Submit Study Data in Logical Observation Identifiers Names and Codes; Notice

FDA (or the Agency) is announcing the extension of the deadline to provide Logical Observation Identifiers Names and Codes (LOINC) for clinical laboratory test results in investigational study data provided in regulatory submissions submitted to CDER and to CBER. FDA has determined, in response to industry comments and internal review, that it is appropriate to extend the date required to submit LOINC codes in NDAs, ANDAs, and BLAs, and for certain INDs. LOINC codes will be required in NDAs, ANDAs, and BLAs for studies that start after March 15, 2020 (March 15, 2021, for certain INDs).

Published October 24, 2017 - Link to FR notice + summary except

- <https://www.gpo.gov/fdsys/pkg/FR-2017-10-24/pdf/2017-23029.pdf> FDA Electronic Study Data Submission; Data Standards; Support for Version Update of World Health Organization Drug Global; Notice

Comments may be submitted to FDA at any time.

FDA (or Agency) is announcing support for the most current B3-format annual version of the World Health Organization (WHO) Drug Global (WHODG) (formerly named WHO Drug Dictionary) (available at <https://www.who.unc.org>), end of support for earlier versions of WHODG, and an update to the FDA Data Standards Catalog (Catalog) for study data provided in NDAs, ANDAs, BLAs, and certain INDs to CBER and CDER.

FDA support for earlier versions of WHODG will end for studies that start after March 15, 2019. The Catalog will be updated to list March 15, 2019, as the “date support ends.” Studies that start after March 15, 2019, will be required to use the most current B3-format annual version of WHODG.

Published October 18, 2017 – Link to FR notice + summary except

- <https://www.gpo.gov/fdsys/pkg/FR-2017-10-18/pdf/2017-22626.pdf> FDA Center for Devices and Radiological Health: Experiential Learning Program; Notice of availability

Fourth Quarter submission period will be open **September 28 – November 1, 2017 at noon**. See ELP website (<https://www.fda.gov/scienceresearch/sciencecareeropportunities/ucm380676.htm>) for details.

FDA’s CDRH (or Center) is announcing the 2018 Experiential Learning Program (ELP). This training is intended to provide CDRH and other FDA staff with an opportunity to understand laboratory practices, quality system management, patient perspective/input, and challenges that impact the medical device development life cycle. The purpose of this document is to invite medical device industry, academia, and health care facilities, and others to participate in this formal training program for CDRH and other FDA staff, or to contact CDRH for more information regarding the ELP.

Tabled to Next meeting

1. Frances Change – Amgen

We have a prefilled cartridge (containing drug product) that is meant to be used together with a device (does not contain any drug). The device is meant to hold the prefilled cartridge in place for injection of the drug.

The prefilled cartridge and device are packaged separately (not in a kit together). It is my understanding that devices alone without drug product, should not be drug-listed on a SPL file.

However, I would like to get more clarity on combination drug/device products.

Can the team kindly advise:

- a. Does the device need to be also drug-listed if it is meant to be used together to deliver the drug product?
- b. If so, how can I list it? Using "asPartofAssembly" data element? (screenshot below from the current FDA Guidance document "Structured Product Labeling Implementation Guide with Validation Procedures v1.0", Revision 201710130913)

Products sold separately but meant to be used together: when products are used together but packaged separately, the data element <asPartOfAssembly> is used to identify the other product. The products could be drugs or devices.

- c. How do other companies handle similar situations?